

ABSTRACT

The invention provides antibodies that specifically bind a membrane protease complex, the complex consisting of two homodimers of seprase and dipeptidyl peptidase IV (DPPIV), obtained from mammalian, preferably human cell membranes. The antibodies specifically bind the DPPIV protease of the seprase-DPPIV complex. This membrane protease complex resides on cell surface invadopodia at the leading edge of angiogenic endothelia, migratory fibroblasts, and invading cancer cells. The antibodies and immunoconjugates of the invention specifically bind the membrane protease complex at the cell surface invadopodia, yet fail to react with resting cells in adjacent human tissues and blood vessels. These antibodies and immunoconjugates block interaction of collagen matrix with the seprase-DPPIV complex in the invasive cells during angiogenesis and cancer spreading but not that with other endothelia or tumor cells. The invention further provides methods for identifying and of using DPPIV antagonists to inhibit capillary sprouting, angiogenesis and cancer invasion in tumor tissues and metastases. Also provided are therapeutic compositions comprising DPPIV antagonists.